

### **REMARKS**

Applicants thank Examiner Fetterolf for the courtesy extended to their representative, Jane Gunnison, in telephone conversations on August 19 and 20, 2008 regarding the July 31, 2008 Office Communication. During the August 19 call, the Examiner noted that the Office Communication contains an error in that it should have referred to SEQ ID NO: 154 and not to SEQ ID NO: 155. During the August 20 call, the Examiner stated that the claim amendments filed on April 22, 2008 had been entered. Because applicants are not amending the April 22, 2008 Listing of Claims in any way in this response, applicants have not included a Listing of Claims herein [37 C.F.R. § 1.121(c) and MPEP§ 714].

The Office Communication, as corrected by the Examiner (above), states that the amendment filed April 22, 2008 was non-responsive because it presented only claims to non-elected subject matter. Specifically, the Communication states that all of the claims were amended "to be drawn to the nucleic acid sequence of SEQ ID NO: [154]" when applicants had elected the nucleic acid sequence of SEQ ID NO: 90. For the sake of clarity, applicants note that the claims relate to an isolated polynucleotide encoding a variant human cytochrome P450 3A4 having a nucleotide substitution compared to the wild type. The polynucleotide comprising the substitution is described in claim 1 in subparagraph (a) as a polynucleotide comprising 15 nucleotides of SEQ ID NO: 154 wherein the 15 nucleotides comprise SEQ ID NO: 90 (which contains the nucleotide substitution) and in subparagraph (b) as a polynucleotide encoding the amino acid sequence in SEQ ID NO: 155 (which contains the corresponding amino acid substitution). SEQ ID NO: 154 is a nucleotide sequence that encodes the amino acid sequence in SEQ ID NO: 155.

During the August 19 call, the Examiner stated that the Office Communication was proper because applicants should have explained the connection between SEQ ID NO: 154, SEQ ID NO: 155 and SEQ ID NO: 90. Applicants believe that the Examiner may have overlooked the statement in their April 22, 2008 reply that: "SEQ ID NO: 155 is encoded by SEQ ID NO: 154 (see, e.g., original claim 1(a)), which comprises SEQ ID NO: 90." (April 22, 2008 Amendment and Response, p. 8. Applicants believe, thus, that their April 22, 2008 reply was fully responsive and that the Office Communication was issued in error. Accordingly, applicants request withdrawal of the Office Communication and appropriate correction to the

Patent Term Adjustment calculation so that applicants do not receive any reduction of the period of adjustment to which they are otherwise entitled in connection with the July 31 Office Communication or the response thereto.

Arguments Filed April 22, 2008

During the August 20, 2008 telephone call, the Examiner requested that applicants include the arguments filed with their April 22, 2008 reply in the response to the Office Communication. Accordingly, applicants have copied those arguments again here for the Examiner's convenience.

APRIL 22, 2008 REMARKS

Applicants have canceled claim 3, without prejudice, have amended claims 1, 4, 6, 8, 12, 37, 39 and 40 and have added claim 41. Applicants expressly reserve the right to pursue any canceled subject matter in one or more applications that claim priority under 35 U.S.C. § 120 from this application.

Specifically, applicants have amended claim 1 to improve its form. Claim 1(a), as amended, recites an isolated polynucleotide comprising 15 nucleotides of SEQ ID NO: 154, wherein the 15 nucleotides comprise the sequence in SEQ ID NO: 90. Support for this amendment may be found in the application, as filed, for example at page 27, lines 26-29 and in original claim 37. Applicants have amended claim 37 to improve its form and have amended claim 40 to be directed to a diagnostic composition comprising a polynucleotide of claim 1. Claim 41 is directed to an isolated polynucleotide comprising a 15-mer identified by recited position numbers in SEQ ID NO. 154 or a polynucleotide comprising a sequence complementary to any one of the recited 15-mers. Each of the 15-mers referred to in subparagraphs (a) to (o) comprises the C→T substitution in Exon 11 described in the application as the M5 variant. See, e.g., Example 5 and Table 3.

None of the amendments adds new matter. Upon entry of the amendments, claims 1, 4-8, 12, 13, 37 and 39 to 41 will be pending in the application. Applicants request entry of the amendments and reconsideration and allowance of the pending claims.

Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 1, 3-8, 12, 13, 37, 39 and 40 stand rejected under 35 U.S.C. § 112, second paragraph as "indefinite." Specifically, in the Examiner's view, claim 1(c) is unclear because it recites a polynucleotide that comprises a sequence corresponding to SEQ ID NO: 90 and comprises a T at a position corresponding to position 6 of SEQ ID NO: 90. The Examiner notes that SEQ ID NO: 90 has a T at position 6.

Similarly, claim 1(e) is said to be unclear because it recites a polynucleotide that encodes a polypeptide, where the polypeptide comprises a sequence corresponding to SEQ ID NO: 155 and comprises an amino acid substitution from T to M at the position that corresponds to position 21 of SEQ ID NO: 155. The Examiner notes that SEQ ID NO: 155 already has an M at position 21. The Examiner states that the subparagraphs (c) and (e) will be interpreted for prior art purposes as a polynucleotide comprising SEQ ID NO: 90 and a polynucleotide encoding a polypeptide comprising SEQ ID NO: 155, respectively. Applicants' cancellation of claim 3, without prejudice, obviates the rejection as to that claim. In view of the claim amendments, applicants traverse as to the remaining claims.

Subparagraph (c) of claim 1, as amended, differs from subparagraph (a) in that (a) recites a polynucleotide comprising a 15-mer that encompasses SEQ ID NO: 90, which does in fact have a T at position 6, as noted by the examiner. Subparagraph (c), on the other hand, is directed to a polynucleotide comprising a 15-mer that encompasses a T at a position that corresponds to position 6 of SEQ ID NO: 90. The specification, as filed, makes clear, that a "corresponding position" as used in the claims means that the location of the position takes into consideration the flanking nucleotides/amino acids and that a "corresponding position" might have a different position number compared to a reference sequence due to deletions or additions elsewhere in the polynucleotide or might be flanked by sequences containing substitutions. Such a "corresponding position" is still identifiable by the flanking nucleotides/amino acids. Claim 1(c), thus, is directed to a polynucleotide that comprises a sequence that need not comprise exactly SEQ ID NO: 90 but can comprise a sequence that has one or more differences from SEQ ID NO: 90 such as a deletion, addition or other substitution. The "position that corresponds to position 6 in SEQ ID NO: 90", thus, may not be the sixth position but nonetheless is identifiable based on similar flanking sequences, and is a T. The same is true *mutatis mutandi* for claim 1 (d).

Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 1, 3-8, 12, 13, 37, 39 and 40 stand rejected under 35 U.S.C. § 112, first paragraph, as containing new matter. In the Examiner's view, the limitations in subparagraphs (c)-(e) of claim 1 are not supported in the application as filed. Applicants' cancellation of claim 3, without prejudice, obviates the rejection as to that claim. In view of the claim amendments, applicants traverse as to the remaining claims.

The application, as filed, states that the invention encompasses a polynucleotide that encodes CYP 3A4 polypeptide that in turn comprises SEQ ID NO: 155. See for example (p. 12, first full paragraph). SEQ ID NO: 155 is encoded by SEQ ID NO: 154 (see, e.g., original claim 1(a)), which comprises SEQ ID NO: 90. The application, as filed, also states that a polynucleotide of the invention may comprise deletions, additions and/or substitutions that were in the prior art (p. 12, last paragraph). Such a polynucleotide and polypeptide, i.e., one encompassing one or more mutations discovered by applicants and disclose herein or other mutations, would be a polynucleotide (or a polypeptide) with a sequence having a position "corresponding to" position 6 of SEQ ID NO: 90. For example, SEQ ID NO: 90 spans nucleotides 166-175 of SEQ ID NO: 154 and contains a novel C→T SNP at position 171. The application, as filed, identifies a further novel SNP at position 172, which also falls within the boundaries of SEQ ID NO: 90. The application, as filed, states that a polynucleotide of the invention can comprise one or more SNPs. SEQ ID NO: 90 with SNPs at positions 6 and 7, thus, is supported in the application, as filed. Such a polynucleotide would "correspond" to SEQ ID NO: 90.

Claims 39 and 40 also stand rejected under § 112, first paragraph (enablement). In the Examiner's view, the specification does not provide enablement for a pharmaceutical composition comprising a polynucleotide of claim 1 or 3. In view of the claim amendments, applicants traverse.

Applicants have canceled claim 3, without prejudice, and have amended claim 40 to refer only to a diagnostic composition. Accordingly, applicants request that the rejection of claims 39 and 40 as lacking enablement be withdrawn.

Rejections under 35 U.S.C. § 102

Claims 1, 3-8, 12, 13, 37, 38 and 40 stand rejected under 35 U.S.C. § 102(e) as “anticipated” by Larossa et al. (U.S. Patent No. 6,025,131) (“Larossa”). Claim 37 stands rejected under 35 U.S.C. § 102(e) as “anticipated” by Mittman et al. (U.S. Patent No. 6,821,724) (“Mittman”). The Examiner continues to contend that Larossa teaches a polynucleotide of claim 1, as well as a vector comprising said polynucleotide, host cells comprising said vector, a nucleic acid molecule complementary to said polynucleotide, a diagnostic composition comprising said polynucleotide, and a method for producing cells comprising said polynucleotide. The Examiner also maintains that Mittman refers to a nucleic acid probe as claimed in claim 37. In view of the claim amendments, applicants traverse.

Claim 1 (and claims 4-8, 12, 13, 37, 38 and 40 by dependency) as amended, recites in pertinent part an isolated polynucleotide comprising 15-mer taken from SEQ ID NO: 154. Larossa does not disclose a polynucleotide comprising 15 nucleotides of SEQ ID NO: 154. Mittman does not disclose a sequence fully complementary to 15 nucleotides from SEQ ID NO: 154.

CONCLUSION

In view of the foregoing, applicants request reconsideration and allowance of the pending claims. Applicants invite the Examiner to contact applicants' representatives at the number below if the Examiner believes that a discussion with would resolve any remaining concerns.

Respectfully submitted,



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